

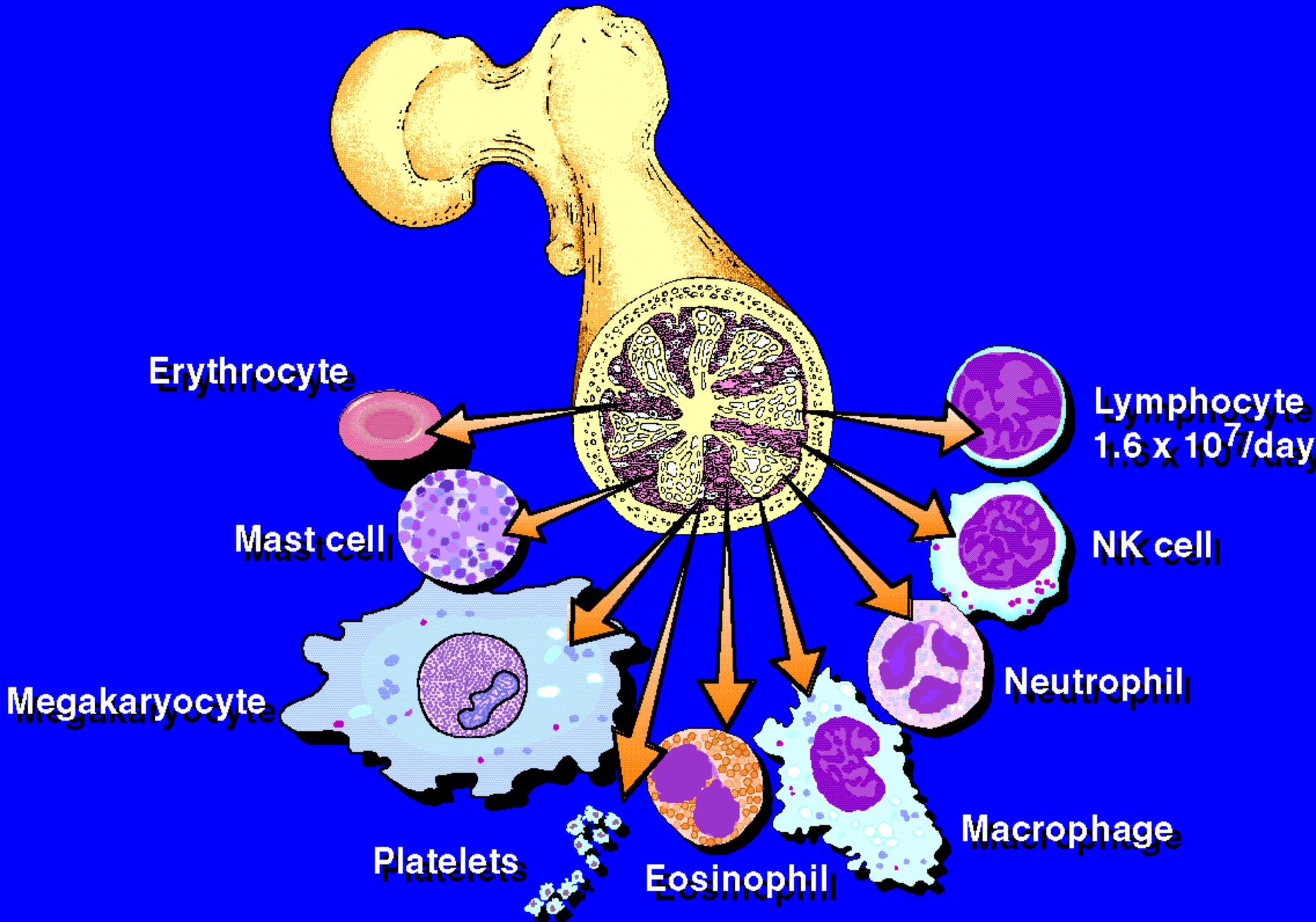
# Workshop Discussion: Biology of the Perimenopause

Paul W. Kincade, Ph.D.

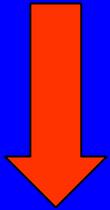


## **What we know:**

- **Sex steroids have a major influence on replenishment of the immune system.**



# B Lymphopoiesis



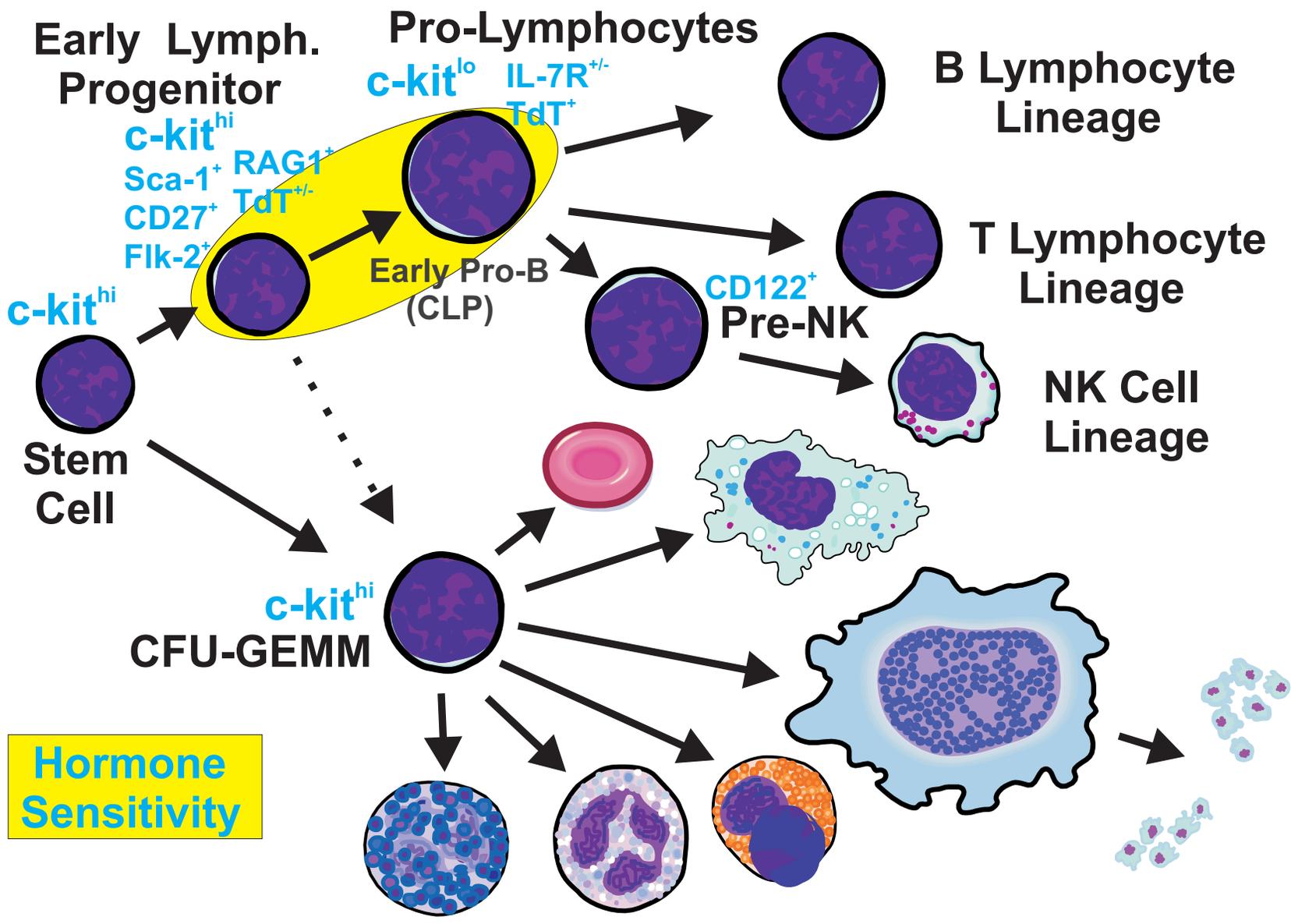
Pregnancy  
E2 Treatment  
Dex Treatment



Castration  
Ovariectomy  
Adrenalectomy  
RU486 Rx  
Hpg/Hpg  
Tfm

## **What we know:**

- **Sex steroids have a major influence on replenishment of the immune system.**
- **Rare lymphoid progenitors and stromal cells are influenced by sex steroids.**

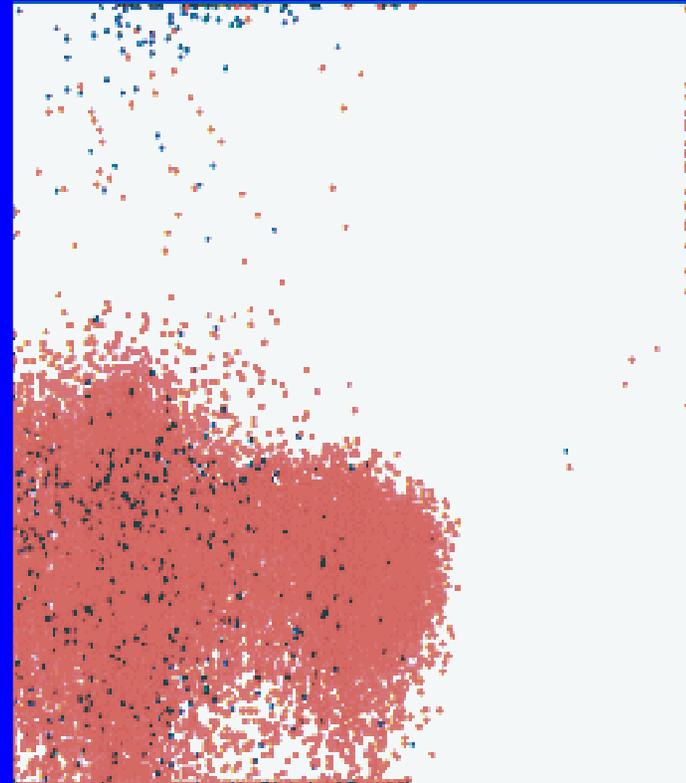
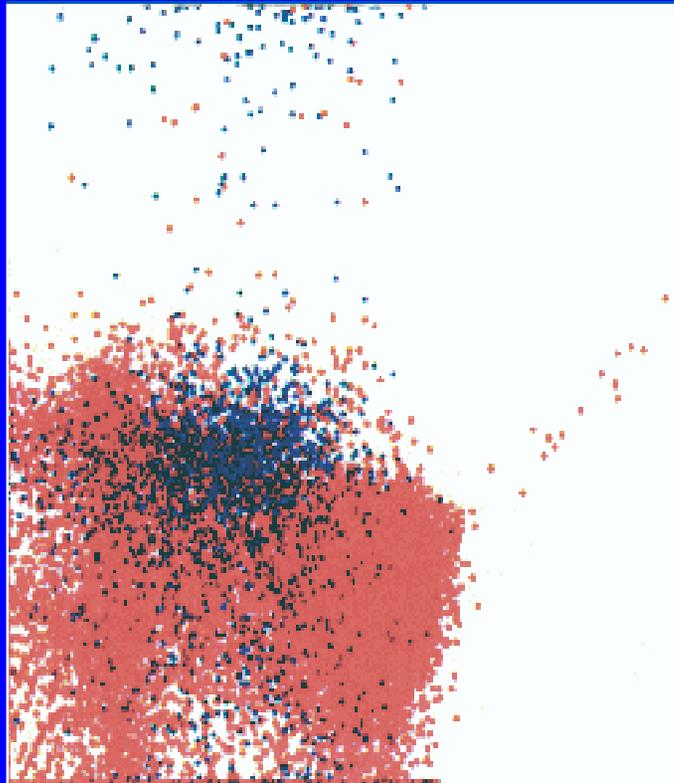


# Early Pro-B Cells\* are Hormone Sensitive

Control

E2 RX

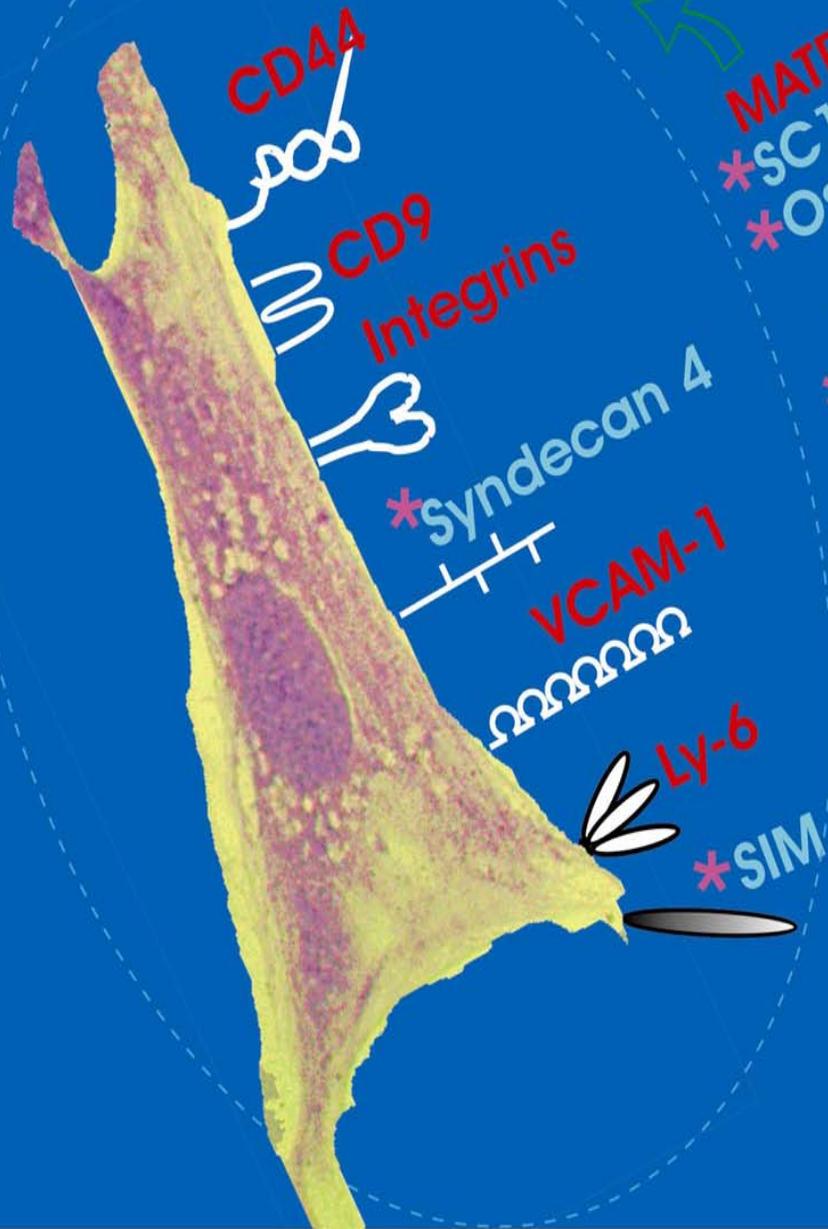
IL-7R



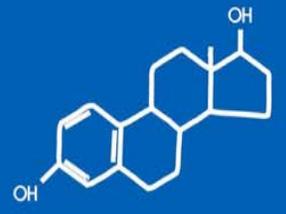
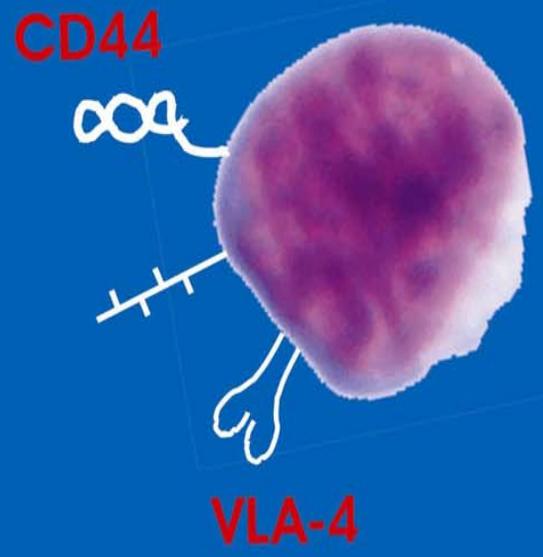
c-Kit

\*Lin<sup>-</sup> TdT<sup>+</sup> Pro-lymphocytes are painted blue.

Notch Family  
Wnt Family



- MATRIX**
- \*SC1
  - \*Osteonectin
  - Thrombospondin
  - Hyaluronan
  - \*Collagens
  - \*Biglycan
  - Fibronectin
  - Laminin
  - Tenascin
  - \*Clusterin

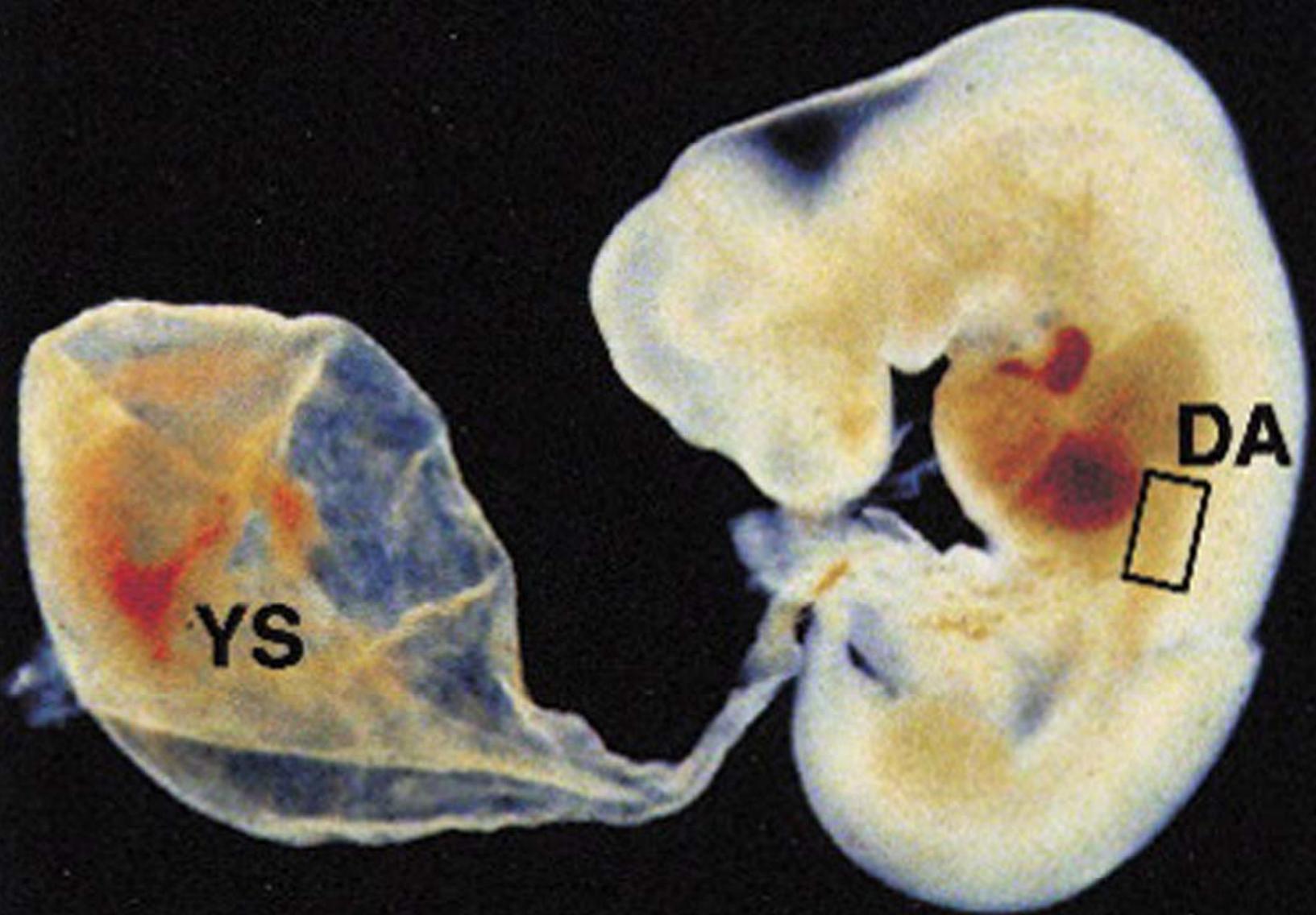


Estrogen

Immobilized/secreted: IL-7, G/M-CSF, IL-3, FGF, PDGF, SCF, TGF- $\beta$ , IFN $\beta$ , limitin, VIP Chemokines

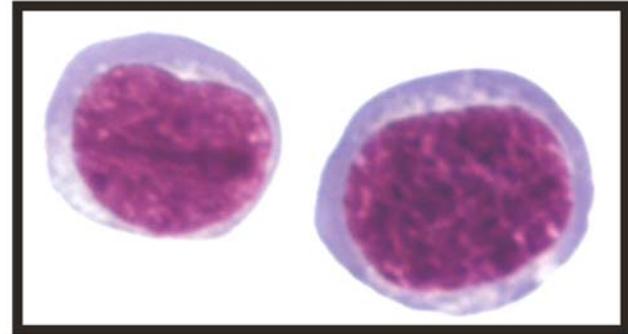
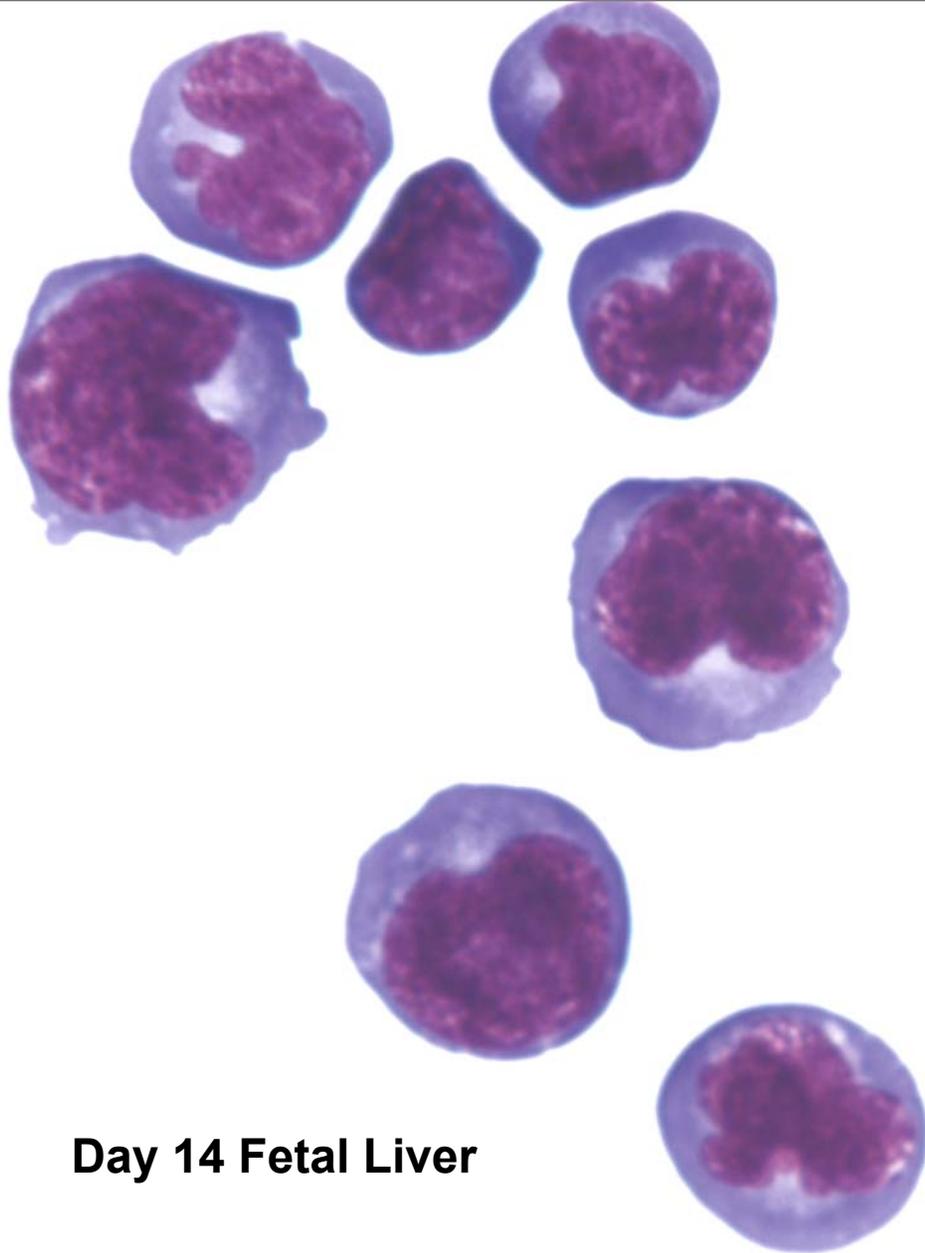
## **What we know:**

- **Sex steroids have a major influence on replenishment of the immune system.**
- **Rare lymphoid progenitors and stromal cells are influenced by sex steroids.**
- **This is only the case in adult life.**

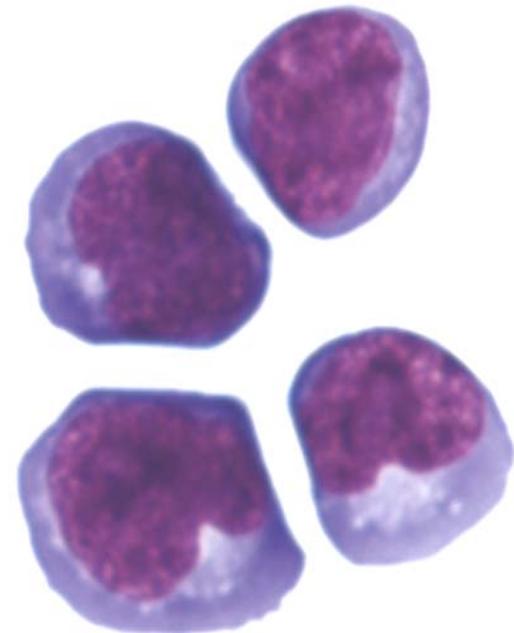


*Traver D. and Zon L.I. Cell 108:731 (2002)*

# GFP<sup>Lo</sup> c-kit<sup>Hi</sup> Sca-1<sup>+</sup> cells



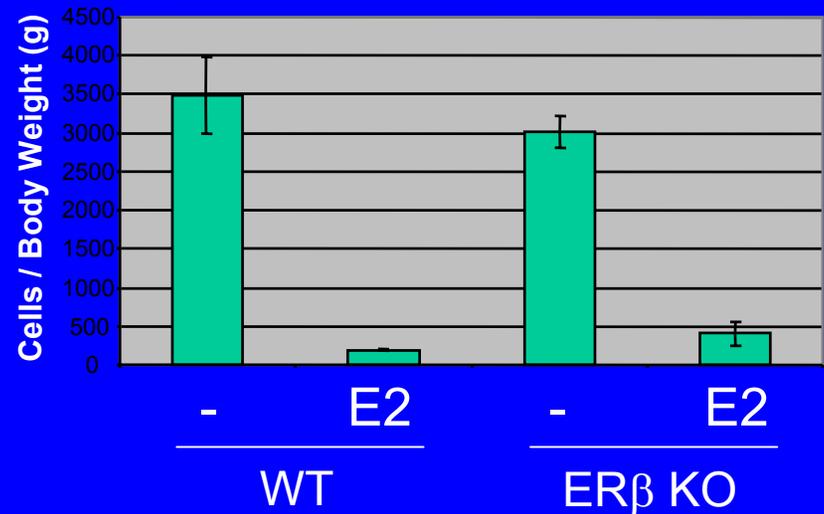
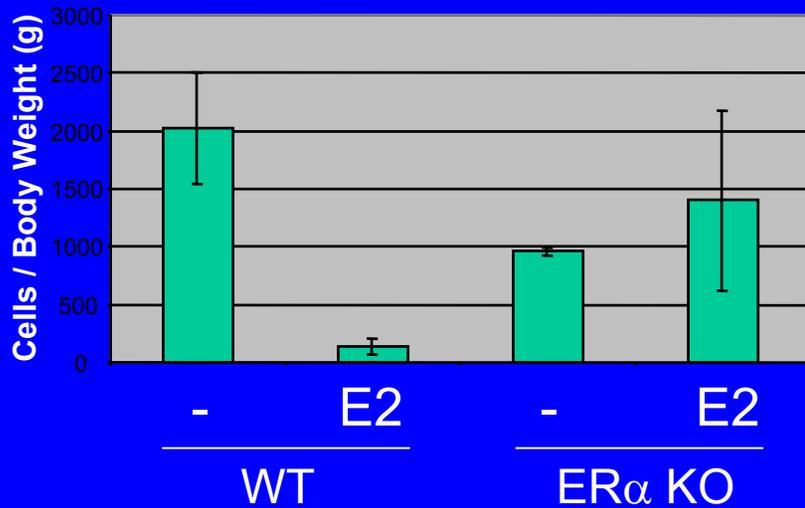
Bone Marrow



## What we know:

- Sex steroids have a major influence on replenishment of the immune system.
- Rare lymphoid progenitors and stromal cells are influenced by sex steroids.
- This is only the case in adult life.
- ER $\alpha$  is particularly important for estrogen responses.

# Estrogen Receptor $\alpha$ , But not ER $\beta$ is Important for Suppression of B Lymphopoiesis by Estrogen

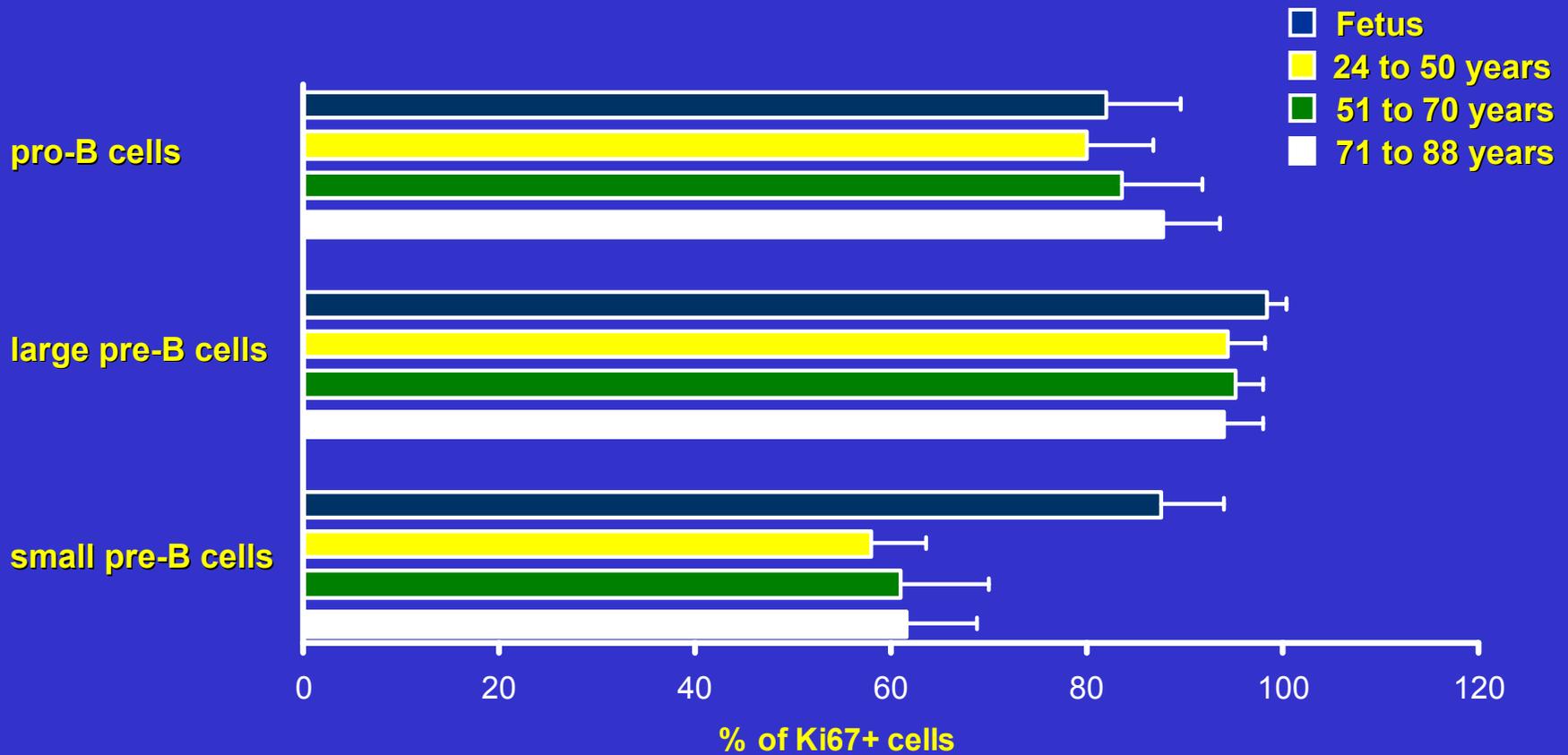


■ Lin<sup>-</sup> TdT<sup>+</sup> Cells  
In Bone Marrow

## What we know:

- **Sex steroids have a major influence on replenishment of the immune system.**
- **Rare lymphoid progenitors and stromal cells are influenced by sex steroids.**
- **This is only the case in adult life.**
- **ER $\alpha$  is particularly important for estrogen responses.**
- **New lymphocytes are made in the bone marrow throughout life. Male/female differences are not apparent.**

# Mitotic Activity of B Lymphocyte Precursors in Normal Human Bone Marrow



## **What we don't know:**

- **Precise mechanisms for hormonal regulation of lymphocyte formation.**
- **Hormone withdrawal in mice increases lymphocyte production. Humans?**
- **Components of the mature immune system in mice are influenced by sex steroids. Significant in post-menopausal women?**